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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,150	07/30/2003	Dah Shiam Chiaur	5914-098-999	1870

20583 7590 07/22/2008

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
07/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,150	CHIAUR ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-76* is/are pending in the application.

4a) Of the above claim(s) *56-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-55,75 and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/03/3008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response received on 04/03/2008 has been entered. Claims 1-49 were cancelled. Claims 50-76 are pending. Claims 51 and 52 are amended. Claims 75 and 76 are newly added.

Claims 56-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 50-55, 75, and 76 are currently under examination.

Specification

Applicant filed amendments to the specification on o4/03/2008 as follows:

The present application is a divisional application of U.S. Patent Application No. 09/385,219, filed August 27, 1999, now U.S. Patent No. 6,720,181, which claims priority under 35 U.S.C. §119 to U.S. Provisional Patent Application No. 60/098,355, filed August 28, 1998, U.S. Provisional Patent Application No. 60/118,568, f]led February 3, 1999, and U.S. Provisional Patent Application No. 60/124,449, filed March 15, 1999, the contents of which are incorporated herein by reference in their entirety.

Priority date

As stated on pages 2-3 of the office action mailed on 10/04/2007, the subject matter of claims 50-55 of instant application requires nucleotide sequence of SEQ ID No: 9 (2076 nucleotides) that encodes the amino acid sequences of SEQ ID No: 10 (447 amino acid residues), asserted to be FBP5. The SEQ ID No: 9 and SEQ ID No: 10 of instant application are identical

to the SEQ ID No: 9 and SEQ ID No: 10 disclosed in the parent application 09/385,219, filed on 08/27/1999, now US patent 6,720,181.

It was noted that the provisional application 60/098,355 filed on 08/28/1998 disclosed SEQ ID No: 10 (447 amino acid residues, see Fig, 7B, page 155 of 60/098,355) that is identical to SEQ ID No: 10 of instant application. However, SEQ ID No: 9, a cDNA encodes FBP5, disclosed in the provisional application 60/098,355 is 1409 nucleotide-long ending with TGA (See Fig, 7A, page 154 of 60/098,355), which is much shorter than SEQ ID No: 9 (2076 nucleotides) disclosed in instant application. Additional provisional application 60/118,568 filed on 02/03/1999 and 60/124,449 filed on 03/13/1999 disclosed the same SEQ ID No: 9, a cDNA encodes FBP5, as that disclosed in the provisional application 60/098,355.

Therefore, the priority date of claim 50 and newly added claim 76 of instant application benefits from the priority dated back to the filing date of provisional application 60/098,355, 08/28/1998 because claim 50 only requires disclosure of SEQ ID No: 10 (447 amino acid residues).

Newly added claim 75 recites "a nucleotide sequence that is at least 25 consecutive nucleotides from nucleotide position 1 to nucleotide position 1409 of SEQ ID NO: 9, which encodes an F-box polypeptide, or a fragment thereof". Accordingly, the priority date of claim 75 is determined to be 08/28/1998, which is the filing date of U.S. Provisional Patent Application No. 60/098,355.

The priority date of claims 51-55 was determined to be 08/27/1999, the filing date of parent application 09/385,219, now patent 6,720,181 as support for SEQ ID NO: 9 of the instant

application is not found in either US Provisional Application 60/098,355 (filed on 08/28/1998), 60/118,568 (filed on 02/03/1999), or 60/124,449 (filed on 03/15/1999).

Claim Rejection - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claims 50-55 remain rejected and newly added claims 76 and 77 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Applicant's arguments filed 04/03/2008 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 3-7 of the office action mailed on 12/01/2006.

In response to the Examiner's question pertaining to the relationship between SEQ ID NO: 19 and SEQ ID NO: 9, as both SEQ ID NO: 19 and SEQ ID NO: 9 are identified as corresponding to FBP5 in the specification at page 8, line 3, and at page 9, lines 5-6, respectively (see page 7 of office action mailed on 10/04/2007), Applicant indicates that SEQ ID NO: 19, which is referred to on page 8, line 3, corresponds to the amino acid sequence of the F-box motif of FBP5, which is a portion of FBP5, as recited in SEQ ID NO: 9. Applicant clarifies that the description of Figure 1 states "Alignment of the conserved F-box motif amino acid residues in the human F-box proteins..." (See, the specification at page 8, lines 1 to 2), and that the specification teaches that SEQ ID NO: 9 corresponds to the cDNA sequence of FBP5 (see, the specification at page 9, lines 6 to 7). Applicant's clarification is acknowledged and appreciated.

Applicant's arguments

With regard to whether nucleotide sequence SEQ ID No: 9 (which is asserted to encode amino acid SEQ ID No: 10) has credible, specific, and substantial utility, Applicant argues the following:

(i) The Examiner has applied an incorrect legal standard for satisfying 35 U.S.C. § 101. The standard for satisfying the utility requirement is not whether the nucleic acid molecules of the present invention encode a functional ubiquitin ligase. The utility requirement under 35 U.S.C. § 101 does not equate to requiring that the nucleic acid molecules of the present invention have to encode a functional ubiquitin ligase (see bridging paragraph pages 7-8, Applicant's response filed on 04/03/2008);

(ii) As discussed previously, the nucleic acid molecules of the present invention do have a specific DNA target, which encodes a novel ubiquitin ligase subunit F box protein 5 ("FBP5"), comprising an F-box motif. Thus, the nucleic acid molecules of the present invention do have a specific utility (see second paragraph page 8, Applicant's response filed on 04/03/2008);

(iii) The specification discloses that F- box proteins, which are subunits of ubiquitin ligases that contain a motif, the F-box, which interacts with Skp1 (see, e.g., the specification at page 2, lines 20 to 28). The specification also teaches that F-box proteins play a role in the ubiquitin pathway and the regulation of the G1 phase of the cell cycle. Therefore, F-box proteins may be useful for the treatment of proliferation and differentiative disorders (see, e.g. the specification at page 58, lines 27 to page 59, line 36). Thus, unlike inventions that contain only a general statement of utility for unspecified diseases, the nucleic acid molecules of the present

invention have a specific utility (see second paragraph page 8, Applicant's response filed on 04/03/2008);

(iv) FBP5 was identified in a yeast 2-hybrid screen for its ability to interact with Skp1 (see. e.g., the specification at page 72, line 1 to page 78, line 28). Sequence analysis of the nucleic acid encoding FBP5 (SEQ ID NO: 9) revealed the presence of an F- box motif and immuno-precipitation experiments confirmed that FBP5 can interact with Skp1 (see, e.g., the specification at page 78, lines 29 to 32; page 80, lines 1 to 9). Accordingly, the specification has provided further evidence that FBP5 is an F-box protein that does indeed interact with the components of the ubiquitin ligase complex. These teachings in the specification thus exceed the threshold requirement of specific utility and substantial utility (see first paragraph page 9, Applicant's response filed on 04/03/2008);

(v) As discussed previously, deregulation of FBPs is implicated in cancer development (see, e.g., the specification at pages 3, line 3 to page 4, line 7; Amendment, filed June 1, 2007, page 6-7). The specification teaches that the nucleic acid molecules of the present invention can be used as probes for detecting FBP5. The specification also teaches that the FBP5 nucleic acid of the present invention is mapped and localized to chromosome position 6q25-26, a region shown to be a site of loss of heterozygosity in human ovarian, breast, and gastric cancer hepatocarcinomas, Burkitt's lymphomas, gliomas, and parathyroid adenomas (see. e.g., the specification at page 56, lines 8 to 14). The specification on page 57, lines 8-25 further teaches that FBP5 can be detected by hybridization assays (e.g., Northern blots, in situ-hybridization). Translocations, deletions and point mutations of FBP5 can be detected by Southern blotting, FISH, RFLP analysis, SSCP, and PCR. The specification further teaches that the protein encoded

by SEQ ID NO: 9 may be used as an immunogen to generate antibodies which immunospecifically bind FBP5

Response to Applicant's arguments

The Examiner agrees with the Applicant's arguments that the standard for satisfying the utility requirement is not whether the nucleic acid molecules of the present invention encode a functional ubiquitin ligase *per se*. However, FBP5 as set forth in SEQ ID NO: 10, which is encoded by nucleic acid sequences set forth in SEQ ID NO: 9, is asserted to be a functional ubiquitin ligase throughout the specification. The Examiner acknowledges that the specification does provide circumstantial evidences indicate that SEQ ID NO: 10 encoded by SEQ ID NO: 9 may encode a functional ubiquitin ligase because the specification discloses that (1) part of SEQ ID NO: 9 was initially identified by yeast two-hybrid as an interacting partner of Skp1, (2) FBP5 as set forth in SEQ ID NO: 10 can interact with Skp1 in immuno-precipitation experiments, and SEQ ID NO: 10 contains a F-box motif, which is present in many proteins whose functions are involved in regulation of protein degradation and cell cycle progression (3) FBP5 nucleic acid of the present invention is mapped and localized to chromosome position 6q25-26, a region shown to be a site of loss of heterozygosity in human ovarian, breast, and gastric cancer hepato-carcinomas, Burkitt's lymphomas, gliomas, and parathyroid adenomas. However, none of these circumstantial evidences unambiguously demonstrates any known function of the isolated and asserted human FBP5 gene, which is asserted to encode an ubiquitin ligase. The specification provides no specific teachings with regard to the function of the protein encoded by the FBP5 gene, and thus, accordingly, an asserted gene defined by nucleic acid sequences set forth in SEQ ID NO: 9 that can encode a protein as set forth in SEQ ID NO: 10, which has no known function,

does not provide specific or substantial utility, as discussed of record advanced on pages 3-7 of the office action mailed on 12/01/2006. It is worth noting that the disclosed interactions between FBP5 polypeptide and Skp1 in two-hybrid screening and immuno-precipitation experiments are not indicative of a functional ubiquitin ligase, and do not provide guidance for the unknown function of the FBP5 polypeptide. These interactions merely provide a starting point for further investigation to reveal the possible function of the FBP5 polypeptide. Applicant's arguments that translocations, deletions and point mutations of FBP5 can be detected by Southern blotting, FISH, RFLP analysis, SSCP, and PCR as specific or substantial utility because of the loss of heterozygosity (LOH) in human ovarian, breast, and gastric cancer hepatocarcinomas, Burkitt's lymphomas, gliomas, and parathyroid adenomas within the chromosome position 6q25-26, are found not persuasive. In this regard, it is noted that the specification does not disclose how many genes (or ORFs, open reading frames) are located with chromosome position 6q25-26 and whether the loss of heterozygosity in the abovementioned diseases is located with in the claimed FBP5 gene (SEQ ID NO: 9) in a statically significant manner. Thus, in order to determine a specific utility for the claimed nucleic acid molecule, the skilled artisan would need to perform further research upon the claimed nucleic acid molecule, in order to determine any correlation between FBP5 function, ubiquitin ligase function, and any of the above-recited diseases. If the function of the gene or its encoded protein are not known in the art, nor disclosed by the specification at the time of filing, then the utility of the claimed invention is not apparent.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Previous rejection of claim 52 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is ***withdrawn*** because the claim has been amended.

Claim 52 has been amended to recite "wherein said highly stringent conditions comprise hybridization in a buffer consisting of 0.5M NaHP04, 7% sodium dodecyl sulfate (SDS), lmM EDTA at 65°C, and washing in a buffer consisting of 0.1xSSC/0.1% SDS at 68°C".

3. Claim 51-55 and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *This rejection is necessitated by claim amendments filed on 04/03/2008.*

It is unclear whether the clause "which encodes an F-box polypeptide, or a fragment thereof" recited in claim 51 and 75 is modifying "SEQ ID NO: 9" or "a nucleotide sequence that is at least 25 consecutive nucleotides of SEQ ID NO: 9", or "an isolated nucleic acid molecule". Claims 53-55 depend from claim 51.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Previous rejection of claims 52-55 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is ***withdrawn*** because Applicant's Arguments in combination with claim amendments have been fully considered and found persuasive.

Claim 52 has been amended to recite "wherein said highly stringent conditions comprise hybridization in a buffer consisting of 0.5M NaHP04, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in a buffer consisting of 0.1xSSC/0.1% SDS at 68°C".

Applicant argues the following: (i) The specification also teaches several assays to confirm the specificity of interaction between the FBPs identified via Yeast Two-Hybrid Screening and human Skp1; (ii) Translated FLAG-tagged FBPs were tested for binding to His-tagged Skp1 pre- bound to Nickel-agarose beads (see, e.g., the specification at page 75, lines l0 to 18; page 80, lines 1 to 9); (iii) The specification also teaches an in vivo assay for determining the interaction of a candidate FBP with Skp1, wherein FLAG-tagged FBP is expressed in Hela cells from which cell extracts are made and subjected to immuno-precipitation with an anti-FLAG antibody (see, e.g., the specification at page 80, lines 15 to 23). Skp1 is then detected in an immunoblot with a specific antibody to Skp1 (see. e.g., the specification at page 80, lines 15 to 23). Thus, Applicant concludes that the specification teaches binding assays for an F-box protein and Skp1.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Previous rejection of claims 51-55 under 35 U.S.C. 102(b) as being anticipated by **Skowyra et al.** (Skowyra et al., F-box proteins are receptors that recruit phosphorylated substrates to the SCF ubiquitin-ligase complex. *Cell*, 91(2): 209-19, 1997) is withdrawn because Applicant's Arguments in combination with claim amendments have been fully considered and found persuasive.

Claim 51 has been amended to recite "a nucleotide sequence that is at least 25 consecutive nucleotides of SEQ ID NO: 9".

Claim 52 has been amended to recite "wherein said highly stringent conditions comprise hybridization in a buffer consisting of 0.5M NaHP04, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in a buffer consisting of 0.1xSSC/0.1% SDS at 68°C".

Applicant argues that Skowyra et al. does not teach an isolated nucleic acid molecule comprising a nucleotide sequence that is at least 25 consecutive nucleotides of SEQ ID NO: 9, which encodes an F-box polypeptide, or a fragment thereof, as recited in claim 51. Applicant argues that sequence alignments of SEQ ID NO: 9 SEQ ID NO: 9 with yeast Cdc4 cDNA and yeast Grr1 cDNA were performed using the LALIGN program which finds the best local alignments between SEQ ID NO: 9 and yeast Cdc4 cDNA; and between SEQ ID NO: 9 and

yeast Grr1 cDNA are less than 25 consecutive nucleotides in length (Exhibit A). Thus, Applicant argues that the nucleotide sequences of yeast Cdc4 and yeast Grr1 do not comprise a nucleotide sequence of SEQ ID NO: 9 that is at least 25 nucleotides in length nor would they hybridize under recited highly stringent conditions to the nucleotide sequence of SEQ ID NO: 9.

6. Claims 51-55 are rejected under 35 U.S.C. 102(e) as being anticipated by Reed et al. (US patent 6,638,734, issued 10/28/2003, effective filing date 06/11/1999). *This rejection is necessitated by claim amendment filed on 04/03/2008.*

It is noted that the priority date of claims 51-55 is 08/27/1999, the filing date of parent application 09/385,219, now patent 6,720,181. Moreover, claim 51 has been amended to recite "a nucleotide sequence that is at least 25 consecutive nucleotides of SEQ ID NO: 9", which no longer requires full length of SEQ ID NO: 9 --- a 2076 nucleotide-long polynucleotide. The limitation "binds to Skp1" recited in claim 52 is the inherent property of the amino acid sequences, which is not considered for patentable weight.

Reed et al. teaches SEQ ID NO: 13 that share 96.7% identical sequences with SEQ ID NO: 9 of instant application (see alignment below, Qy, query; Db, database). Reed et al. teaches expression vector and host cell for expression of disclosed sequences (See lines 47-58, col. 14, Reed et al., 2003). Reed et al. teaches high stringency hybridization (See lines 32-40, col. 8) and the 2030 identical nucleotide sequences between SEQ ID NO: 13 disclosed by Reed et al. and SEQ ID NO: 9 of instant application, will inherently hybridize to SEQ ID NO: 9 of instant application under the highly stringent hybridization recited in claim 52. Claims 53-55 depend from claims 51 or 52.

Thus, Reed et al. clearly anticipate claims 51-55 of instant application.

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RESULT 3
US-09-591-694-13
; Sequence 13, Application US/09591694
; Patent No. 6638734
; GENERAL INFORMATION:
;  APPLICANT: John C. Reed
;  APPLICANT: Shu-ichi Matsuzawa
;  TITLE OF INVENTION: Nucleic Acid Encoding Proteins Involved
;  TITLE OF INVENTION: in Protein Degradation, Products and Methods Related Thereto
;  FILE REFERENCE: P-LJ 4220
;  CURRENT APPLICATION NUMBER: US/09/591,694
;  CURRENT FILING DATE: 2000-06-09
;  EARLIER APPLICATION NUMBER: US 09/330,517
;  EARLIER FILING DATE: 1999-06-11
;  NUMBER OF SEQ ID NOS: 49
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 13
;  LENGTH: 2037
;  TYPE: DNA
;  ORGANISM: Homo sapien
;  FEATURE:
;  NAME/KEY: CDS
;  LOCATION: (70)...(1410)
US-09-591-694-13

  Query Match             96.7%;  Score 2008.4;  DB 3;  Length 2037;
  Best Local Similarity   99.7%;  Pred. No. 0;
  Matches 2023;  Conservative    0;  Mismatches    6;  Indels    1;  Gaps    1;

Qy          1 AGGTTGCTCAGCTGCCCCGGAGCGGTTCCTCCACCTGAGGCAGACACCACCTCGGTTGG 60
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Db          9 AGGTTGCTCAGCTGCCCCGGAGCGGTTCCTCCACCTGAGGCAGACTCCACGTCGGCTGG 68

Qy         61 CATGAGCCGGCGCCCCTGCAGCTGCGCCCTACGGCCACCCCGCTGCTCCTGCAGCGCCAG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         69 CATGAGCCGGCGCCCTGCAGCTGCGCCCTACGGCCACCCCGCTGCTCCTGCAGCGCCAG 128

Qy        121 CCCCAGCGCAGTGACAGCCGCCGGGCGCCCTCGACCCTCGGATAGTTGTAAAGAAGAAAG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        129 CCCCAGCGCAGTGACAGCCGCCGGGCGCCCTCGACCCTCGGATAGTTGTAAAGAAGAAAG 188

Qy        181 TTCTACCCTTTCTGTCAAAATGAAGTGTGATTTTAATTGTAACCATGTTCATTCCGGACT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        189 TTCTACCCTTTCTGTCAAAATGAAGTGTGATTTTAATTGTAACCATGTTCATTCCGGACT 248

Qy        241 TAAACTGGTAAAACCTGATGACATTGGAAGACTAGTTTCCTACACCCCTGCATATCTGGA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        249 TAAACTGGTAAAACCTGATGACATTGGAAGACTAGTTTCCTACACCCCTGCATATTTGGA 308

Qy        301 AGGTTCCTGTAAAGACTGCATTAAAGACTATGAAAGGCTGTCATGTATTGGGTCACCGAT 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        309 AGGTTCCTGTAAAGACTGCATTAAAGACTATGAAAGGCTGTCATGTATTGGGTCACCGAT 368

Qy        361 TGTGAGCCCTAGGATTGTACAACTTGAAACTGAAAGCAAGCGCTTGCATAACAAGGAAAA 420
              ||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||
Db        369 TGTGAGCCCTAGGATTGTAAAACTTGAAACTGAAAGCAAGCGCTTGCATAACAAGGAAAA 428

Qy        421 TCAACATGTGCAACAGACACTTAATAGTACAAATGAAATAGAAGCACTAGAGACCAGTAG 480
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Qy        481 ACTTTATGAAGACAGTGGCTATTCCTCATTTTCTCTACAAAGTGGCCTCAGTGAACATGA 540
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Db        489 ACTTTATGAAGACAGTGGCTATTCCTCATTTTCTCTACAAAGTGGCCTCAGTGAACATGA 548

Qy        541 AGAAGGTAGCCTCCTGGAGGAGAATTTCGGTGACAGTCTACAATCCTGCCTGCTACAAAT 600
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Db        549 AGAAGGTAGCCTCCTGGAGGAGAATTTCGGTGACAGTCTACAATCCTGCCTGCTACAAAT 608

Qy        601 ACAAAGCCCAGACCAATATCCCAACAAAAACTTGCTGCCAGTTCTTCATTTTGAAAAAGT 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        609 ACAAAGCCCAGACCAATATCCCAACAAAAACTTGCTGCCAGTTCTTCATTTTGAAAAAGT 668

Qy        661 GGTTTGTTCAACATTAAAAAAGAATGCAAAACGAAATCCTAAAGTAGATCGGGAGATGCT 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        669 GGTTTGTTCAACATTAAAAAAGAATGCAAAACGAAATCCTAAAGTAGATCGGGAGATGCT 728

Qy        721 GAAGGAAATTATAGCCAGAGGAAATTTTAGACTGCAGAATATAATTGGCAGAAAAATGGG 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        729 GAAGGAAATTATAGCCAGAGGAAATTTAGACTGCAGAATATAATTGGCAGAAAAATGGG 788

Qy        781 CCTAGAATGTGTAGATATTCTCAGCGAACTCTTTCGAAGGGACTCAGACATGTCTTAGC 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        789 CCTAGAATGTGTAGATATTCTCAGCGAACTCTTTCGAAGGGACTCAGACATGTCTTAGC 848

Qy        841 AACTATTTTACACACAACTCAGTGACATGGACTTAATCAATGTGTCTAAAGTGAGCACAAC 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        849 AACTATTTTACACACAACTCAGTGACATGGACTTAATCAATGTGTCTAAAGTGAGCACAAC 908

Qy        901 TTGGAAGAAGATCCTAGAAGATGATAAGGGGGCATTCCAGTTGTACAGTAAAGCAATACA 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        909 TTGGAAGAAGATCCTAGAAGATGATAAGGGGGCATTCCAGTTGTACAGTAAAGCAATACA 968

Qy        961 AAGAGTTACCGAAAACAACAATAAATTTTCACCTCATGCTTCAACCAGAGAATATGTTAT 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        969 AAGAGTTACCGAAAACAACAATAAATTTTCACCTCATGCTTCAACCAGAGAATATGTTAT 1028

Qy       1021 GTTCAGAACCCCACTGGCTTCTGTTCAGAAATCAGCAGCCCAGACTTCTCTCAAAAAAGA 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1029 GTTCAGAACCCCACTGGCTTCTGTTCAGAAATCAGCAGCCCAGACTTCTCTCAAAAAAGA 1088

Qy       1081 TGCTCAAACCAAGTTATCCAATCAAGGTGATCAGAAAGGTTCTACTTATAGTCGACACAA 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1089 TGCTCAAACCAAGTTATCCAATCAAGGTGATCAGAAAGGTTCTACTTATAGTCGACACAA 1148

Qy       1141 TGAATTCTCTGAGGTTGCCAAGACATTGAAAAAGAACGAAAGCCTCAAAGCCTGTATTCG 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1149 TGAATTCTCTGAGGTTGCCAAGACATTGAAAAAGAACGAAAGCCTCAAAGCCTGTATTCG 1208

Qy       1201 CTGTAATTCACCTGCAAAATATGATTGCTATTTACAACGGGCAACCTGCAAACGAGAAGG 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1209 CTGTAATTCACCTGCAAAATATGATTGCTATTTACAACGGGCAACCTGCAAACGAGAAGG 1268

Qy       1261 CTGTGGATTTGATTATTGTACGAAGTGTCTCTGTAATTATCATACTACTAAAGACTGTTC 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1269 CTGTGGATTTGATTATTGTACGAAGTGTCTCTGTAATTATCATACTACTAAAGACTGTTC 1328

Qy       1321 AGATGGCAAGCTCCTCAAAGCCAGTTGTAAAATAGGTCCCCTGCCTGGTACAAAGAAAAG 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1329 AGATGGCAAGCTCCTCAAAGCCAGTTGTAAAATAGGTCCCCTGCCTGGTACAAAGAAAAG 1388

Qy       1381 CAAAAAGAATTTACGAAGATTGTGATCTCTTATTAAATCAATTGTTACTGATCATGAATG 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1389 CAAAAAGAATTTACGAAGATTGTGATCTCTTATTAAATCAATTGTTACTGATCATGAATG 1448

Qy       1441 TTAGTTAGAAAAATGTTAGGTTTTAACTTAAAAAAAATTGTATTGTGATTTTCAATTTTAT 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1449 TTAGTTAGAAAAATGTTAGGTTTTAACTTAAAAAAAATTGTATTGTGATTTTCAATTTTAT 1508

Qy       1501 GTTGAAATCGGTGTAGTATCCTGAGGTTTTTTTCCCCCCAGAAGATAAAGAGGATAGACA 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1509 GTTGAAATCGGTGTAGTATCCTGAGGTTTTTTTCCCCCCAGAAGATAAAGAGGATAGACA 1568

Qy       1561 ACCTCTTAAAATATTTTACAATTTAATGAGAAAAAGTTTAAAATTCTCAATACAAATCA 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1569 ACCTCTTAAAATATTTTACAATTTAATGAGAAAAAGTTTAAAATTCTCAATACAAATCA 1628

Qy       1621 AACAATTTAAATATTTAAGAAAAAAGGAAAAGTAGATAGTGATACTGAGGGTAAAAAAA 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1629 AACAATTTAAATATTTAAGAAAAAAGGAAAAGTAGATAGTGATACTGAGGGT-AAAAAA 1687

Qy       1681 AAATTGATTCAATTTTATGGTAAAGGAAACCCATGCAATTTTACCTAGACAGTCTTAAAT 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1688 AAATTGATTCAATTTTATGGTAAAGGAAACCCATGCAATTTTACCTAGACAGTCTTAAAT 1747

Qy       1741 ATGTCTGGTTTTCCATCTGTTAGCATTTCAGACATTTTATGTTCCTCTTACTCAATTGAT 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1748 ATGTCTGGTTTTCCATCTGTTAGCATTTCAGACATTTTATGTTCCTCTTACTCAATTGAT 1807

Qy       1801 ACCAACAGAAATATCAACTTCTGGAGTCTATTAAATGTGTTGTCACCTTTCTAAAGCTTT 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1808 ACCAACAGAAATATCAACTTCTGGAGTCTATTAAATGTGTTGTCACCTTTCTAAAGCTTT 1867

Qy       1861 TTTTCATTGTGTGTATTTCCCAAGAAAGTATCCTTTGTAAAAACTTGCTTGTTTTCCTTA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1868 TTTTCATTGTGTGTATTTCCCAAGAAAGTATCCTTTGTAAAAACTTGCTTGTTTTCCTTA 1927

Qy       1921 TTTCTGAAATCTGTTTTAATATTTTTGTATACATGTAAATATTTCTGTATTTTTATATG 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1928 TTTCTGAAATCTGTTTTAATATTTTTGTATACATGTAAATATTTCTGTATTTTTATATG 1987

Qy       1981 TCAAAGAATATGTCTCTTGTATGTACATATAAAAATAAATTTTGCTCAAT 2030
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Db       1988 TCAAAGAATATGTCTCTTGTATGTACATATAAAAATAAATTTTGCTCAAT 2037
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7. Claims 51-55, 75 and 76 are rejected under 35 U.S.C. 102(e) as being anticipated by Williams et al. (US patent 6,964,868, issued 11/15/2005, effective filing date 01/28/1998). This rejection is necessitated by claim amendment filed on 04/03/2008.

It is noted that the priority date of claim 51 is 08/27/1999, the filing date of parent application 09/385,219, now patent 6,720,181. The priority date of claim 75 is determined to be 08/28/1998, which is the filing date of U.S. Provisional Patent Application No. 60/098,355.

Claim 51 has been amended to recite "a nucleotide sequence that is at least 25 consecutive nucleotides of SEQ ID NO: 9", which no longer requires full length of SEQ ID NO: 9 --- a 2076 nucleotide-long polynucleotide. Claims 53-55 depend from claims 51 or 52. Newly added claim 75 recites "a nucleotide sequence that is at least 25 consecutive nucleotides from nucleotide position 1 to nucleotide position 1409 of SEQ ID NO: 9".

It is noted that the limitation "at least about 95% similarity to SEQ ID NO: 10" recited in claim 76 does not require full length SEQ ID NO: 10. The limitation "binds to Skp1" recited in claims 52 and 76 is the inherent property of the amino acid sequences, which is not considered for patentable weight.

Williams et al. teaches SEQ ID NO: 13 that share 96.7% identical sequences with the nucleotide sequences starting from position 712 to position 1220 of SEQ ID NO: 9 of instant application (see alignment below, Qy, query; Db, database). The ~ 400 identical nucleotide sequences between SEQ ID NO: 13 disclosed by Reed et al. and SEQ ID NO: 9 of instant application, will inherently hybridize to SEQ ID NO: 9 of instant application under the highly

stringent hybridization recited in claim 52. Williams et al. teaches expression vector and host cell for expression of disclosed sequences (See claims 2, 3, 8, and 9, Williams et al., 2005).

Thus, Reed et al. clearly anticipate claims 51-55, 75 and 76 of instant application.

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RESULT 5
US-09-297-648-4117
; Sequence 4117, Application US/09297648
; Patent No. 6964868
; GENERAL INFORMATION:
;  APPLICANT:  Williams, Lewis T.
;  APPLICANT:  Escobedo, Jaime
;  APPLICANT:  Innis, Michael A.
;  APPLICANT:  Garcia, Pablo Dominiquez
;  APPLICANT:  Sudduth-Klinger, Julie
;  APPLICANT:  Reinhard, Christoph
;  APPLICANT:  Glese, Klause
;  APPLICANT:  Randazzo, Filippo
;  APPLICANT:  Kennedy, Giulia C.
;  APPLICANT:  Pot, David
;  APPLICANT:  Kassan, Altaf
;  APPLICANT:  Lamson, George
;  APPLICANT:  Drmanac, Radoje
;  APPLICANT:  Crkvenjakov, Radomir
;  APPLICANT:  Dickson, Mark
;  APPLICANT:  Drmanac, Snezana
;  APPLICANT:  Labat, Ivan
;  APPLICANT:  Leshkowitz, Dena
;  APPLICANT:  Kita, David
;  APPLICANT:  Garcia, Veronica
;  APPLICANT:  Jones, William Lee
;  APPLICANT:  Stache-Crain, Birjit
;  TITLE OF INVENTION:  No. 6964868el Human Genes and Gene Expression
;  TITLE OF INVENTION:  Products II
;  FILE REFERENCE:  2300-1481
;  CURRENT APPLICATION NUMBER:  US/09/297,648
;  CURRENT FILING DATE:  2000-03-10
;  PRIOR APPLICATION NUMBER:  60/072,910
;  PRIOR FILING DATE:  1998-01-28
;  PRIOR APPLICATION NUMBER:  60/075,954
;  PRIOR FILING DATE:  1998-02-24
;  PRIOR APPLICATION NUMBER:  60/080,666
;  PRIOR FILING DATE:  1998-04-03
;  PRIOR APPLICATION NUMBER:  60/080,515
;  PRIOR FILING DATE:  1998-04-03
;  PRIOR APPLICATION NUMBER:  60/080,114
;  PRIOR FILING DATE:  1998-03-31
;  PRIOR APPLICATION NUMBER:  60/105,234
;  PRIOR FILING DATE:  1998-10-21
;  NUMBER OF SEQ ID NOS:  5252
;  SOFTWARE:  FastSEQ for Windows Version 4.0
; SEQ ID NO 4117
;   LENGTH: 817
;   TYPE: DNA
;   ORGANISM: Homo sapiens
;   FEATURE:
;   NAME/KEY: misc_feature
;   LOCATION: (1)...(817)
;   OTHER INFORMATION: n = A,T,C or G
US-09-297-648-4117

  Query Match          20.2%;  Score 420;  DB 4;  Length 817;
  Best Local Similarity  88.4%;  Pred. No. 2.3e-90;
  Matches  450;  Conservative    0;  Mismatches   59;  Indels    0;  Gaps    0;

Qy        712 GGAGATGCTGAAGGAAATTATAGCCAGAGGAAATTTTAGACTGCAGAATATAATTGGCAG 771
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         68 GGAGATGCTGAAGGAAATTATAGCCAGAGGAAATTTTAGACTGCAGAATATAATTGGCAG 127

Qy        772 AAAAATGGGCCTAGAATGTGTAGATATTCTCAGCGAACTCTTTCGAAGGGGACTCAGACA 831
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        128 AAAAATGGGCCTAGAATGTGTAGATATTCTCAGCGAACTCTTTCGAAGGGGACTCAGACA 187

Qy        832 TGTCTTAGCAACTATTTTAGCACAACTCAGTGACATGGACTTAATCAATGTGTCTAAAGT 891
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        188 TGTCTTAGCAACTATTTTAGCACAACTCAGTGACATGGACTTAATCAATGTGTCTAAAGT 247
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Qy         892 GAGCACAACTTGGAAGAAGATCCTAGAAGATGATAAGGGGGCATTCCAGTTGTACAGTAA 951
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         248 GAGCACAACTTGGAAGAAGATCCTAGAAGATGATAAGGGGGCATTCCAGTTGTACAGTAA 307

Qy         952 AGCAATACAAAGAGTTACCGAAAACAACAATAAATTTTCACCTCATGCTTCAACCAGAGA 1011
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         308 AGCAATACAAAGAGTTACCGAAAACAACAATAAATTTTCACCTCATGCTTCAACCAGAGA 367

Qy        1012 ATATGTTATGTTCAGAACCCCACTGGCTTCTGTTCAGAAATCAGCAGCCCAGACTTCTCT 1071
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         368 ATATGTTATGTTCAGAACCCCACTGGCTTCTGTTCAGAAATCAGCAGCCCAGACTTCTCT 427

Qy        1072 CAAAAAAGATGCTCAAACCAAGTTATCCAATCAAGGTGATCAGAAAGGTTCTACTTATAG 1131
               |||||||||||||||||||||||||||||||||||||||||||||| | ||||||||| |
Db         428 CAAAAAAGATGCTCAAACCAAGTTATCCAATCAAGGTGATCAGAAANGGTCTACTTATTG 487

Qy        1132 TCGACACAATGAATTCTCTGAGGTTGCCAAGACATTGAAAAAGAACGAAAGCCTCAAAGC 1191
               ||              | |   |  |       |     |  |||  ||   |  |||||
Db         488 TCCGACACCATNGAANTNTTTTGAGGGTTGCNAAANACCATTGAAAAAAGAACNAAAAGC 547

Qy        1192 CTGTATTCGCTGTAATTCACCTGCAAAAT 1220
               ||  |    |     ||| | || ||| |
Db         548 CTTAAAAGCCCTGTNTTCNCTTGTAAATT 576
```

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Thaian N. Ton/
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